PATENT SPECIFICATION

654,860

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COMPLETE SPECIFICATION

Improvements in or relating to Therapeutic Medication

We, ABBOTT LABORATORIES, a corporation duly organized under the laws of the State of Illinois, United States of America, of 14th Street and Sheriden Road, City of North Chicago, County of Lake, State of Illinois, United States of America, do hereby declare the nature of this invention and in what manner the same is to be performed, to be particularly described and ascertained in and by the following statement:—

Our invention relates to therapeutic medication and includes among its objects and advantages increased convenience in medication with dry medicaments in powder form, especially with respect to accuracy of dosage and accurate placement of the material.

Many useful medicaments, and especially penicillin and related antibiotics, are subject to substantial or, in some instances, complete alteration by the stomach juices when administered orally. Different patients vary widely in the condition of the alimentary canal and the extent to which oral dosages will be impaired in effectiveness. In fact, the same patient will react differently to the same dosage at different times, because the condition of the patient's alimentary canal varies from time to time.

On this account, precision in treatment has only been attainable in the past with oral dosages supplemented by checking blood samples to ascertain how much medicament has found its way into the blood stream, or by parenteral administration.

It has been discovered that the airborne ingestion of powdered penicillin and other medicaments available in the form of fine powders, can be practised to cause therapeutic effects. It is also possible to combine the general treatment thus resulting with high local concentration of the same medicament in whatever body cavity is utilized.

In addition to water-soluble antibiotics, solid inhalation therapy is of value in connection with other therapeutic agents, including antiseptics, bronchiolytics, and vaso-constrictors, and is indicated for at least some of the known anti-histamine drugs. Illustrative examples of vaso-constrictors are: epinephrine hydrochloride, isopropyl epinephrin and 2-amino-heptane. Illustrative examples of anti-histamine agents are: N-(Alpha-pyridyl)-N-(alphathenyl)-N^1, N^1-dimethylethylenediamine hydrochloride, and N-(alpha-pyridyl)-N-(benzyl)-N^1, N^1-dimethylethylenediamine hydrochloride.

Data available so far does not support any reliable generalizations. More particularly, the mere fact that a drug is ineffective or toxic when administered orally affords no indication whether or not it is suitable for solid inhalation therapy. Many such therapeutic agents which are water soluble, will be found effective by solid inhalation, but both the effect and the degree of effectiveness need to be established by specific test in connection with each substance.

However, especially when the local application is in the lungs, a wide variability in the proportion of powdered material that comes to rest in the nose and in the bronchial tubes and in the actual lung itself can only be avoided by a substantial constancy in the method of inhalation.

By the present invention, such constancy has been obtained by providing apparatus which is to be utilized by the patient by breathing in and out in a simple, substantially normal way. The energy of the patient's breathing is utilized to deliver into each charge of air inhaled, a small substantially constant charge of powdered medicament, which charge is delivered quickly, shortly after inhalation begins, and finds its way to its

[Price 2/-]

resting place long before inhalation is finished. Thus the apparatus itself and the body passages first receiving the stream of air are thoroughly swept and scavenged with pure air during the major portion of the breathing-in process. It has been found that administration in this way not only contributes to deep penetration of the medicament, but that it becomes unnecessary to pulverize the medicament into a true smoke. The use of larger particles tends to increase the reliability with which a uniform fraction of the material will pass on through the body passages first receiving the stream without getting caught on the moist walls.

Whereas other methods of administration by inhalation known to us are objectionable because the apparatus is expensive or complicated, or because the amount of medicament rendered effective for therapeutic purposes varies uncontrollably over a range of several hundred per cent., or both, it is possible according to the invention to work out dependable procedures which do not require hospital treatment or the repeated checking of blood samples.

Apparatus for administering medicament in small particle form by inhalation comprises, according to this invention, a conduit having an air inlet and an air outlet, a container for the medicament suspended in the conduit and means actuated by each inhalation to jolt the container, the container having an outlet permitting a limited discharge into the conduit at each jolting of the container whereby air passing through the conduit becomes medicated. The conduit may comprise an air inlet passage leading from the inlet to the container, a piston member guided in the passage to jolt the container at each inhalation, the suspended container being disposed in relation to the inner end of the passage so that the piston member impacts on the container wall to jolt the container, and openings in the passage constituting a by-pass to the piston when in impacting position permitting air flow through the passage to continue after impact.

In the preferred form of apparatus according to the invention, the inlet passage is of arcuate form, and is disposed in a vertical plane when the apparatus is in use and the piston member is constituted by a ball, the passage enforcing suction effort to be developed in the inhalation volume to raise the ball in the passage and thereby provide a time lag assuring that inhalation commences before the respective discharge of medicament is procured whilst assuring rearward movement of the piston member as soon as the suction applied fails to hold the ball at the top of its excursion path.

The medicament container is preferably suspended within the chamber in proximity to the end of the said passage and the piston member is allowed to partially leave the passage at the end of its forward travel to directly impact on the container, in which impact position the by-pass is uncovered by the piston.

Preferably the container passes loosely through the wall of the chamber so that free play is given to the lugs to permit limited movement of the container on impact therewith by the piston member whereby the container is abruptly arrested in its movement derived from the piston member and a double jolt to the container is obtained.

The invention further consists in the practical embodiments of the invention illustrated in the accompanying drawings in which:—

Figure 1 is a section of an inhalator according to the invention, on line I—I of Figure 2;

Figure 2 is a plan view of the same inhalator from above;

Figure 3 is a section on line III—III of Figure 2;

Figure 4 is a side view of the capsule with the cover removed;

Figure 5 is a section on line IX—IX of Figure 1;

Figure 6 is a section similar to Figure 1, on line VI—VI of Figure 7, indicating a modified construction;

Figure 7 is a plan view partly in section on line VII—VII of Figure 6;

Figure 8 is a section on line VIII—VIII of Figure 7; and

Figure 9 is an end view of the nose end of the modified form.

In the drawings like references designate the same or similar parts.

In the drawings as filed, the parts are substantially to scale and about twice normal size.

In the embodiment of apparatus selected for illustration, the main housing 1 is of transparent plastic molded in two halves and seamed together on the plane of the section of Figure 1. The body defines a chamber 2 in the general shape of an open cup. The upper wall of the body is apertured to receive a capsule containing the medicament 4.

An arcuate pipe 5 forms an inlet passage to the cup which it enters close beside the capsule 3. Outside the cup it curves downwardly and back toward the user to reduce the overall length of the device, and thereby providing an upward incline which reaches the chamber

Within the inlet passage 5 is a piston member constituted by a ball 6 which normally lies at the bottom of the passage 5, being restrained from falling out by the bail 7 of a retaining clip 8. The clip has resilient side arms 9 that set in place between ribs 10 on the tube 5 and curve into shallow pockets 11. A simple steel ball functions very well in this connection, but with a ball of aluminium the parts may be designed to ensure a slightly better mechanical action. When the capsule is in place the ball 6 is restrained from leaving the inlet tube 5 by the capsule itself, but to limit the forward travel of the ball lips 12 are provided with extend in from upper quadrants of the edge of the tube to its inner end. The inner end of the tube comprising the upward incline is also provided with side slots 13 and a bottom slot 14 extending back along the tube far enough so that the ball will pass the rear ends of the slots at the end of its inward movement and thus open inlet apertures for the entrance of air into the cup 2 by by-passing the ball when in impact position.

When sufficient suction has been applied to the chamber to overcome the inertia of the ball, the ball is drawn up the arcuate tube 5 and runs up the incline to impact on the container, and when that amount of suction on the ball ceases, the ball rolls down the incline by gravity and comes to rest on the bail 7. The percussion is thus derived from a movable mass (the ball 6) constrained to travel under the suction effort of aspiration in an upward direction so that the effort required to raise the mass must be developed, and thereby enforce a delay in the production of the percussion until after inhalation has commenced, whilst the body passages of the patient inhaling, which first receive the floated medicament, are scavenged during the subsequent portion of each aspiration. Accordingly the initial part of each volume of inhalation passes through the chamber before medicament is discharged, and then the medicament is borne forward in the remaining part of the inhalation, which also effects scavenging as herein explained.

The capsule 3 which forms the subject matter of the copending application No. 13228/50 (Serial No. 654,872) includes a barrel 15 which houses the medicament 4 retained by a mesh screen 16, a top flange 17 and a knurled operating handle 18.

The capsule is filled at the factory and then covered with the cap 19, the bottom 20 of which bulges up slightly in undistorted position so that when the cap is pushed in place over the capsule the bottom will press snugly against the screen 16.

The flange 17 has opposite ears 21 so that the capsule can be assembled with the body by a bayonet joint connection. As clearly indicated in Figure 1, the body has a bore 22 to receive the barrel 15 with material clearance so that the capsule is loose and can move freely to an appreciable extent. Similarly a groove 23 which receives the flange 17 provides equal or greater clearance for the flange so that the free movement is not impaired. By allowing the free movement of the container in the chamber wall, the container first receives the impact from the ball, then travels with the ball for the tolerance permitted by the mounting of the chamber in the container, and is then arrested by the wall of the container so that a second jar is given to the container. Thereby by such an arrangement a double impact is obtained. A top flange 24 has opposite notches at 25 through which the lugs 21 can be moved axially and the groove 23 is filled in, or interrupted, at 26. Thus the user can move the capsule axially into position, and then turn it in either direction and it will turn 90 degrees and then be arrested between stops 26, so that the user will not inadvertently swing it through 180 degrees where it could fall out.

Detachable connecting means are provided for connecting the cup 1 to a desired body cavity. In Figures 1, 2 and 3 is illustrated a connector for the mouth. The body 1 has an external rabbet and the connector 27 has an internal rabbet. A flange 28 on the body 1 is interrupted in the middle of the top at 29 to define a notch and the connector flange has a filled-in portion at 30 to fit in the notch, so that the connector and body will always be assembled in the same relative positions. The body 27 has converging top and bottom walls and slightly diverging side walls to define a flaring shape ending in a horizontally wide and vertically narrow discharge opening 31 with at least the central portions of the top and bottom wall carrying outwardly directed flanges 32 by which the teeth of the user may comfortably and conveniently be engaged during use.

To use the device, a capsule is inserted as indicated in Figure 1 and the user slips the mouth piece between his lips and takes a deep breath. Because the volume of the body and connector is a negligible fraction of the volume, even a child will inhale in this way, the increment of powder dislodged by the impact of the piston member constituted by the ball

against the capsule will be swept through the chamber and into the body passages and followed by a considerable inhalation of pure air to scavenge both the device and the initial body passages.

Because, with the ball 6 in the full line position of Figure 1, the possible openings for reverse flow of air through the device are extremely constricted, the natural impulse of the user to withdraw the device or to release the lips and breathe out around it, is confirmed and enforced so that the moist air exhaled by the user does not go back through the device to moisten the walls of the chamber and cause the next increment of powder to be retained where it is not desired.

It will be obvious that the connectors can be shaped to fit any body cavity into which the patient can draw air. In Figures 6 to 9 is indicated a nosepiece also of transparent plastic. The portion of the nosepiece engaging the body 1 is of identical configuration with the connector 27, but it has a bifurcated body 33 terminating in spaced lobes 34 of a size or configuration to enter comfortably into the nostrils. The interior clearance is also bifurcated to end in spaced discharge openings 35 positioned to deliver the stream of fluid close to the septum and substantially parallel thereto.

By varying the fineness of the powder and the mesh of the screen 16, various powdered medicaments can be administered at various rates. With sodium penicillin a screen of about 60 mesh is preferred and it is not hard to granulate the powder by trial and error to a grain size such that an administration of 100,000 units is easily accomplished by normal breathing, in from five to ten minutes. We have also found that smoother and more accurate mechanical action can be secured by mixing the penicillin with at least a little other material intended to function as a diluent or vehicle.

Because the energy of the user's breath actuates the timed discharge, there is no other instrumentality with which any synchronism needs to be maintained. Further, because there is no extraneous power imposed on the ingoing air stream, the patient's natural and normal lung movements are not disturbed and upset by being pushed or pulled in a way that is always uncomfortable and frequently unexpected and bad for the morale of the patient.

In the embodiment of Figures 1 to 5, the end of the inlet passage 5 projects slightly through the chamber 12. In the embodiment of Figures 6 to 9 the shape is substantially identical, and the floor 35 of the modified chamber 36 slopes up to and flush with the bottom of the slot 14. The bottom of the cup is flush with the end of the tube 5 and the small corner pockets at the bottom of the chamber 36 are filled in up to inclined planes or interior facets 37. This affords a particle of powder no resting place that is not inclined downwardly and toward the centre so that the air stream entering through the slots 13 and 14 will always keep the lower portions of the chamber well scavenged. This scavenging action is assisted by the fact that the loose fit for the capsule 3 permits material leakage of air which will acquire considerable velocity directly downwards as it passes through the annular clearance around the barrel 15, and tend to direct the main stream downward more or less and assist in keeping the chamber scavenged. The other function of the loose mounting is to permit a substantial movement or displacement of the capsule from the position of Figure 1, in which it is held by gravity, when the ball 6 strikes it, thus providing a more effective jolt to shake a small increment of the powder 4 out through the sieve 16.

The capsule 15 is of such size that it can be housed within the chamber 2 and the body 27 or 33.

While it is contemplated that the capsules will be sold in quantity in separate packages this feature is useful in a large institution where a supply of the devices can be prepared in sterile condition by a student nurse, with a capsule housed in each device for quick use in emergencies, such as acute attacks of asthma.

Having now particularly described and ascertained the nature of our said invention, and in what manner the same is to be performed, we declare that what we claim is:—

1. Apparatus for administering medicament in small particle form by inhalation comprising a conduit having an air inlet and an air outlet, a container for the medicament suspended in the conduit and means actuated by each inhalation to jolt the container, the container having an outlet permitting a limited discharge into the conduit at each jolting of the container whereby air passing through the conduit becomes medicated.

2. Apparatus according to Claim 1 characterised in that the conduit comprises an air inlet passage leading from the inlet to the container, a piston member guided in the passage to jolt the container at each inhalation, the suspended container being disposed in relation to the inner end of the passage so that the

piston member impacts on the container wall to jolt the container, and openings in the passage constituting a by-pass to the piston when in impacting position permitting air flow through the passage to continue after impact.

3. Apparatus according to Claim 2, characterised in that the inlet passage is of arcuate form and is disposed in a vertical plane when the apparatus is in use and the piston member is constituted by a ball, the passage enforcing suction effort to be developed in the inhalation volume to raise the ball in the passage and thereby provide a time lag assuring that inhalation commences before the respective discharge of medicament is procured whilst assuring rearward movement of the piston member as soon as the suction applied fails to hold the ball at the top of its excursion path.

4. Apparatus according to Claims 2 or 3, characterised in that the container is suspended within the chamber in proximity to the end of the said passage and the piston member is allowed to partially leave the passage at the end of its forward travel to directly impact on the contained, in which impact position the bye-pass is uncovered by the piston.

5. Apparatus according to Claim 4 characterised in that the container is suspended within the chamber by lugs, and that the container loosely passes through the wall of the chamber so that free play is given to the lugs to permit limited movement of the container on impact therewith by the piston member, whereby the container is abruptly arrested in its movement derived from the piston member and a double jolt to the container is obtained.

6. Apparatus for administering medicament in particle form by inhalation constructed and arranged substantially as described with reference to Figures 1 to 5 of the accompanying drawings.

7. Apparatus for administering medicament in particle form by inhalation constructed and arranged substantially as described with reference to Figures 6 to 9 of the accompanying drawings.

Dated this 19th day of August, 1948.

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Agents for the Applicants.

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FIG. 1

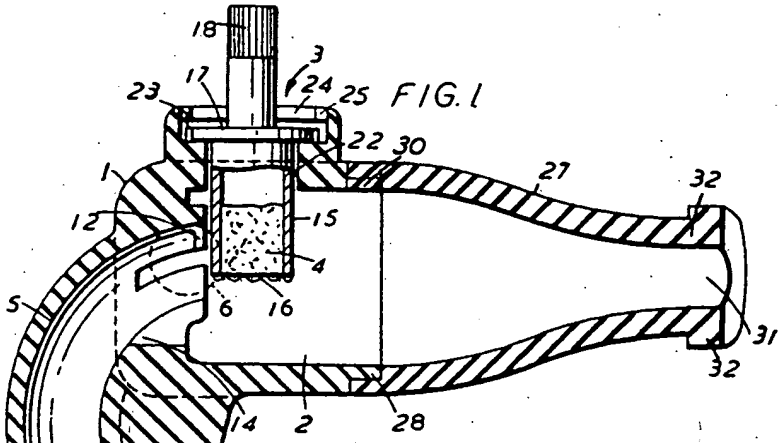


FIG 2

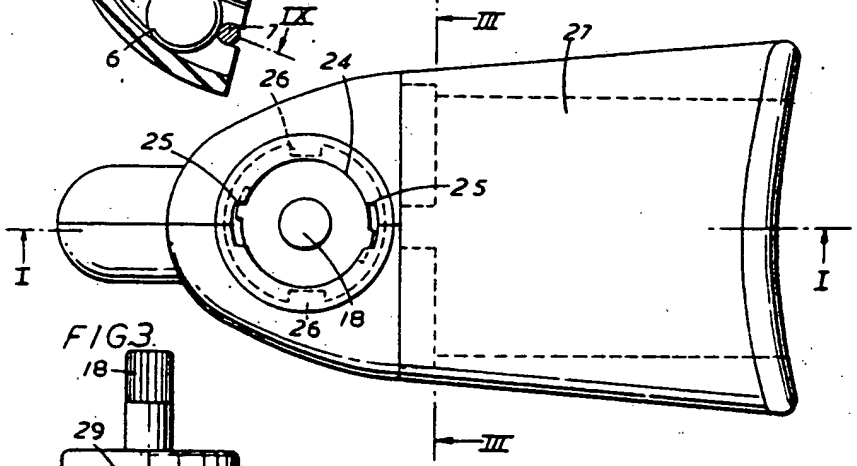
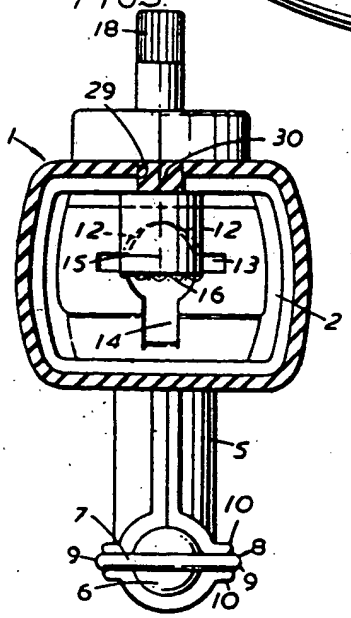


FIG 3



III

FIG 4

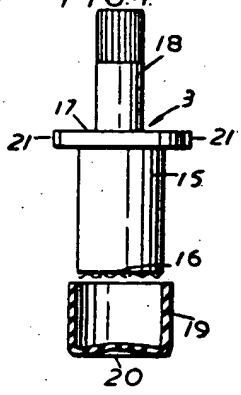
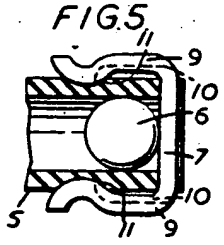
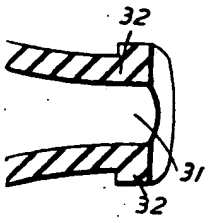


FIG 5





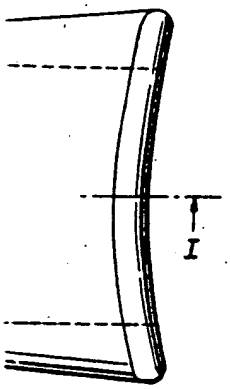


FIG.5

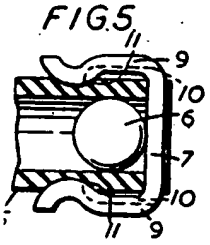


FIG.6.

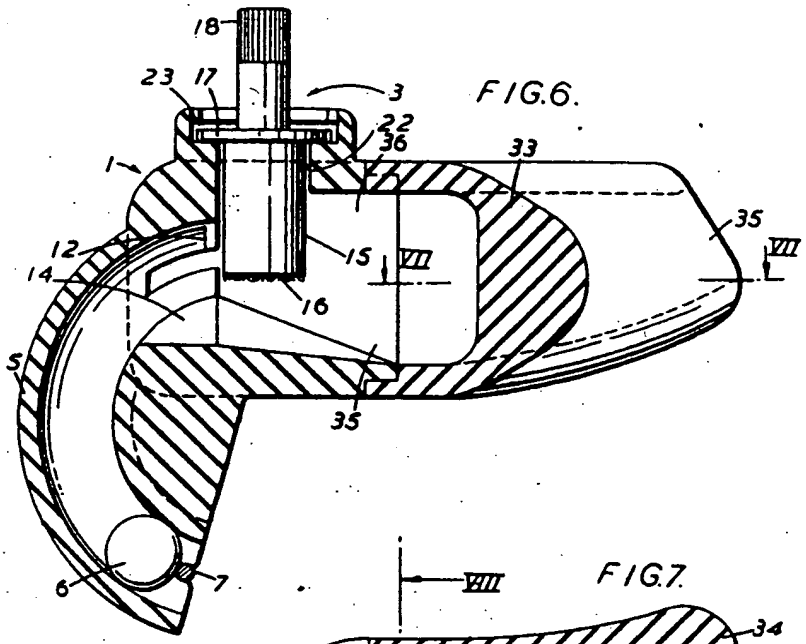


FIG.7.

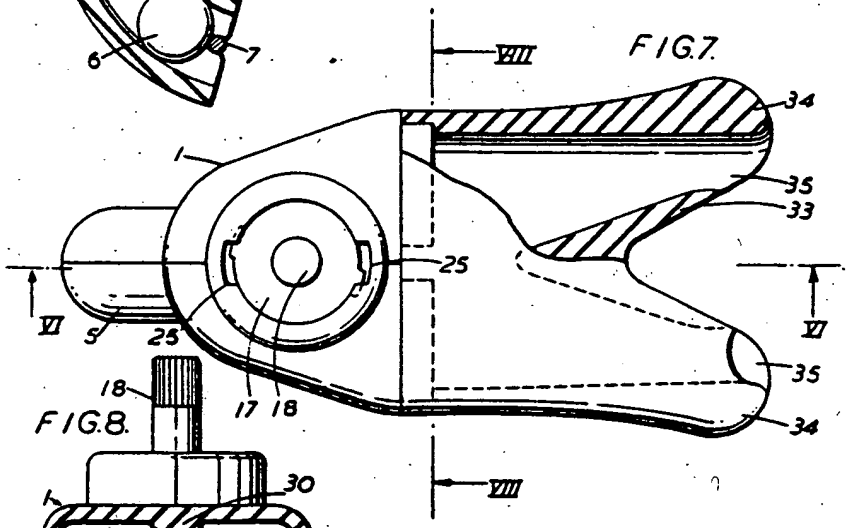


FIG.8.

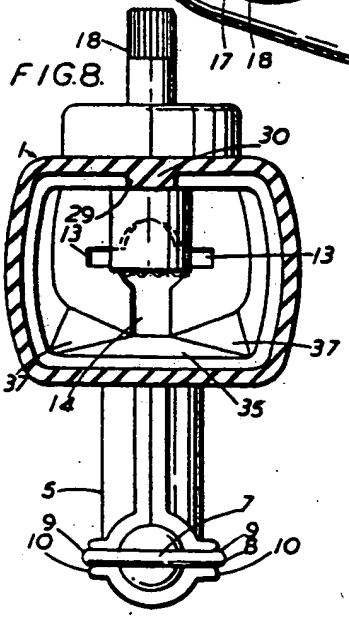
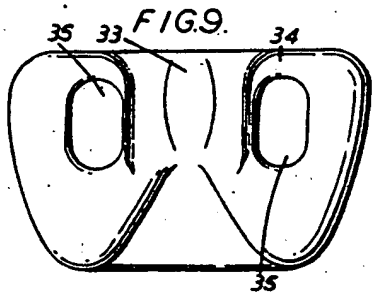


FIG.9.



H.M.S.O. (M.F.P.)